

CLAIMS

1. A purified protein selected from the group consisting of:

(a) a protein which consists of an amino acid sequence represented by any one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178 and 180; and

(b) a protein that activates NF- κ B (Nuclear factor kappa B) and consists of an amino acid sequence having at least one amino acid deletion, substitution or addition in an amino acid sequence represented by any one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178 and 180.

2. A purified protein that activates NF- κ B and comprises an amino acid sequence having at least 95% identity to the protein according to claim 1 over the entire length thereof.

3. An isolated polynucleotide which comprises a nucleotide sequence encoding a protein selected from the group consisting of:

(a) a protein which comprises an amino acid sequence represented by any one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178 and 180; and

(b) a protein that activates NF- κ B and consists of an amino acid sequence having at least one

amino acid deletion, substitution or addition in an amino acid sequence represented by any one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178 and 180.

4. An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of:

(a) a polynucleotide sequence represented by any one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177 and 179;

(b) a polynucleotide sequence encoding a protein that activates NF- κ B and hybridizing under stringent conditions with a polynucleotide having a polynucleotide sequence complementary to the polynucleotide sequence of (a); and

(c) a polynucleotide sequence which encodes a protein that activates NF- κ B and consists of a polynucleotide sequence having at least one nucleotide deletion, substitution or addition in a polynucleotide sequence represented by any one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177 and 179.

5. An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence represented by a coding region in any one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58,

60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177 and 179;

(b) a nucleotide sequence encoding a protein that activates NF- κ B and hybridizing under stringent conditions with a polynucleotide having a polynucleotide sequence complementary to the polynucleotide sequence of (a); and

(c) a nucleotide sequence which encodes a protein that activates NF- κ B and consists of a nucleotide sequence having at least one nucleotide deletion, substitution or addition in a nucleotide sequence represented by a coding region in any one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177 and 179.

6. An isolated polynucleotide comprising a nucleotide sequence which encodes a protein that activates NF- κ B and has at least 95% identity to the polynucleotide sequence according to claim 3 over the entire length thereof.

7. An isolated polynucleotide comprising a nucleotide sequence which encodes a protein that activates NF- κ B and has at least 95% identity to the polynucleotide sequence according to claim 4 or 5 over the entire length thereof.

8. A purified protein encoded by the polynucleotide according to any one of claims 3 to 7.

9. A recombinant vector which comprises a polynucleotide according to any one of claims 3 to 7.

10. A gene therapy agent comprising the recombinant vector according to claim 9 as an

active ingredient.

11. A transformed cell which comprises the recombinant vector according to claim 9.

12. A membrane of the cell according to claim 11, when the protein according to claim 1 or 2 is a membrane protein.

13. A process for producing a protein comprising,

(a) culturing a transformed cell comprising the isolated polynucleotide according to any one of claims 3 to 7 under conditions providing expression of the encoded protein; and

(b) recovering the protein from the culture product.

14. A process for diagnosing a disease or susceptibility to a disease related to expression or activity of the protein of claim 1, 2 or 8 in a subject comprising:

(a) determining the presence or absence of a mutation in the nucleotide sequence encoding said protein in the genome of said subject; and/or

(b) analyzing the amount of expression of said protein in a sample derived from said subject.

15. A method for screening compounds in respect of activity to inhibit or promote NF- κ B activation, which comprises the steps of:

(a) providing a cell with a gene encoding a protein that activates NF- κ B, and a component that provides a detectable signal associated with activation of NF- κ B;

(b) culturing a transformed cell under conditions, which permit the expression of the gene in the transformed cell;

(c) contacting the transformed cell with one or more compounds;

(d) measuring the detectable signal; and

(e) isolating or identifying an activator compound and/or an inhibitor compound by measuring the detectable signal.

16. A process for producing a pharmaceutical composition, which comprises the steps of:

- (a) providing a cell with a gene encoding a protein that activates NF- κ B, and a component capable of providing a detectable signal;
- (b) culturing a transformed cell under conditions, which permit the expression of the gene in the transformed cell;
- (c) contacting the transformed cell with one or more compounds;
- (d) measuring the detectable signal;
- (e) isolating or identifying an activator compound and/or an inhibitor compound by measuring the detectable signal; and
- (f) optimizing the isolated or identified compound as a pharmaceutical composition.

17. A kit for screening a compound in respect of activity to inhibit or promote NF- κ B activation, which comprises:

- (a) a cell comprising a gene encoding a protein that activates NF- κ B, and a component that provides a detectable signal upon activation of NF- κ B; and
- (b) reagents for measuring the detectable signal.

18. A monoclonal or polyclonal antibody or a fragment thereof that specifically binds to the protein according to claim 1, 2 or 8.

19. The monoclonal or polyclonal antibody or a fragment thereof according to claim 18 that inhibits the action of activating NF- κ B of the protein according to claim 1, 2 or 8.

20. A process for producing a monoclonal or polyclonal antibody that specifically binds to the protein according to claim 1, 2 or 8, which comprises administering the protein according to claim 1, 2 or 8 or epitope-bearing fragments thereof to a non-human animal.

21. An antisense oligonucleotide complementary to the polynucleotide according to any one of claims 3 to 7, which prevents NF- κ B activator protein expression.

22. A ribozyme which inhibits NF- κ B activation by cleavage of RNA that encodes the protein according to claim 1, 2 or 8.

23. A double stranded nucleic acid having a nucleotide sequence corresponding to a part of the nucleotide sequence of the isolated polynucleotide according to any one of claims 3-7, which inhibit the expression of the protein that activates NF- κ B.

24. The double stranded nucleic acid according to claim 23, wherein the nucleic acid has a nucleotide sequence corresponding to a part of the nucleotide sequence represented by SEQ ID NO: 88, and inhibits the expression of the protein having the amino acid sequence represented by SEQ ID NO: 87.

25. A double stranded nucleic acid obtained by annealing of any one of the following oligonucleotide pairs (a)-(f):

- (a) 5'- GUCCAGGAUAUCAUGAGUCN_n -3' (SEQ ID NO: 213)
3'- N_nCAGGUCCUAUAGUACUCAG -5' (SEQ ID NO: 214)
- (b) 5'- GAAGUCUGAAGAUCUAUCCN_n -3' (SEQ ID NO: 215)
3'- N_nCUUCAGACUUCUAGAUAGG -5' (SEQ ID NO: 216)
- (c) 5'- GCUGAAGAAGAGGUGUUCCN_n -3' (SEQ ID NO: 217)
3'- N_nCGACUUUCUUCUCCACAAGG -5' (SEQ ID NO: 218)
- (d) 5'- GAUGACACAGAUGAAGGCCN_n -3' (SEQ ID NO: 219)
3'- N_nCUACUGUGUCUACUUCGGG -5' (SEQ ID NO: 220)
- (e) 5'- GCCCUCAGAGGUCCAGAAUCN_n -3' (SEQ ID NO: 221)
3'- N_nCGGGAGUCUCAGGUCUUAG -5' (SEQ ID NO: 222)
- (f) 5'- GAUGACUUUGGUAUCAAACN_n -3' (SEQ ID NO: 223)
3'- N_nCUACUGAAACCAUAGUUUG -5' (SEQ ID NO: 224)

wherein N represents any one of G, A, T, C, and U, and n is 1 to 4.

26. The double stranded nucleic acid according to claim 25, wherein Nn is TT or UU.
27. A double stranded nucleic acid having one or more mutations in the sense strand of the double strand nucleic acid according to claim 26.
28. A double stranded nucleic acid comprising the double stranded nucleic acid according to any one of claims 25 to 27 as a part, which inhibits the expression of the protein having the amino acid sequence represented by SEQ ID NO: 87.
29. An expression vector capable of expressing the double stranded nucleic acid according to claim 25, wherein Nn is UU or UUU.
30. A method for treating a disease, which comprises administering to a subject an amount of compound screened by the process according to claim 15, and/or a monoclonal or polyclonal antibody or a fragment thereof according to claim 18 or 19, and/or an antisense oligonucleotide according to claim 21 and/or a ribozyme according to claim 22 and/or a double stranded nucleic acid according to any one of claims 23-28 and/or the expression vector according to claim 29 effective to treat a disease selected from the group consisting of inflammation, autoimmune diseases, infectious disease, cancers and bone diseases.
31. A method for treating a disease, which comprises administering to a subject an amount of a compound screened by the process according to claim 15, and/or a monoclonal or polyclonal antibody or a fragment thereof according to claim 18 or 19, and/or an antisense oligonucleotide according to claim 21 and/or a ribozyme according to claim 22 effective to treat a disease selected from the group consisting of inflammation, autoimmune diseases, infectious disease, cancers and bone diseases.
32. A pharmaceutical composition produced by the process according to claim 16 as an inhibitor or promoter of NF- κ B activation.

33. A pharmaceutical composition according to claim 32 for the treatment of inflammation, autoimmune diseases, cancers, infectious diseases, bone diseases, AIDS, neurodegenerative diseases or ischemic disorders.

34. A method of treating inflammation, autoimmune diseases, cancers, infectious diseases, bone diseases, AIDS, neurodegenerative diseases, or ischemic disorders, which comprises administering a pharmaceutical composition produced by the process according to claim 16 to a patient suffering from a disease associated with NF- κ B activation.

35. A pharmaceutical composition which comprises a monoclonal or polyclonal antibody or a fragment thereof according to claim 18 or 19 as an active ingredient.

36. A pharmaceutical composition which comprises an antisense oligonucleotide according to claim 21 as an active ingredient.

37. A pharmaceutical composition which comprises a ribozyme according to claim 22 as an active ingredient.

38. A pharmaceutical composition or a gene therapy agent which comprises a double stranded nucleic acid according to any one of claims 23 to 28 and/or an expression vextor according to claim 29 as an active ingredient.

39. An expression inhibiting agent for a protein having an action of activating NF- κ B, which comprises a double stranded nucleic acid according to any one of claims 23 to 28 and/or an expression vextor according to claim 29 as an active ingredient.

40. The pharmaceutical composition according to claim 35 or 36, wherein the target disease is selected from the group consisting of inflammation, autoimmune diseases, infectious

diseases, cancers, bone diseases, AIDS, neurodegenerative and ischemic disorders.

41. A method for obtaining a novel gene having a function, which comprises at least the following steps:

- (a) constructing a full-length cDNA library by the oligo-capping method;
- (b) cotransfected the full-length cDNA and a plasmid containing a factor emitting a signal indicative of the presence of a protein having the function into cells; and
- (c) selecting a plasmid emitting the signal.

42. A computer-readable medium on which a sequence data set has been stored, said sequence data set comprising at least one nucleotide sequence selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177 and 179, and/or at least one amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178 and 180.

43. A method for calculating identity to other nucleotide sequences and/or amino acid sequences, which comprises comparing data on a medium according to claim 42 with data of said other nucleotide sequences and/or amino acid sequences.

44. An insoluble substrate to which polynucleotides comprising all or part of the nucleotide sequences selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64,

66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177 and 179, are fixed.

45. An insoluble substrate to which polypeptides comprising all or a part of the amino acid sequences selected from the group consisting of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178 and 180, are fixed.